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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/525,986	02/25/2005	Tadashi Nakajima	05116/HG	5004

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EXAMINER	
BASQUILL, SEAN M	

ART UNIT	PAPER NUMBER
1613	

MAIL DATE	DELIVERY MODE
03/21/2011	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/525,986	NAKAJIMA ET AL.	
	Examiner	Art Unit	
	SEAN BASQUILL	1613	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 March 2011*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2 and 21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 2, 21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10 March 2011*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 1 March 2011 has been entered.

Previous Rejections

2. Applicants' arguments, filed 1 March 2011, have been fully considered. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. Claims 1, 2 and 21 stand rejected under 35 U.S.C. 103(a) as being unpatentable over EP/0286903A1 ("Bito"), in view of U.S. Patent 7,015,210 ("Aiken"), P. Vasantha Rao, et al, Modulation of Aqueous Humor Outflow Facility by the Rho Kinase-Specific Inhibitor Y-27632,

42 INV. OPHTHALMOL. VIS. SCI. 1029 (April 2001) ("Rao"), U.S. Patent 6,271,224 ("Kapin") (all of record), as put forth in the previous office actions.

Applicants arguments have been fully considered and are deemed unpersuasive. Applicants arguments directed to the purported "teaching away from" the combination proposed by the examiner is would foundation. Even if the applicants interpretation of the Bito reference were to be taken as accurate, a point which the examiner does not concede, applicants arguments fail for the simple reason that the compounds of Aiken would be expected to IMPROVE the intraocular pressure lowering effects of the prostaglandin derivatives. The evidence offered by applicants discusses only the possible vasodilatory effects associated with hydroxy fasudil, and makes absolutely no mention of any effects on intraocular pressure. For this reason alone, applicants evidence fails to even support the argument advanced, namely that a rho kinase inhibitor would interfere with the IOP lowering effect of a prostaglandin derivative.

Indeed, part of the reason that the Rho kinase inhibitors of Rao and Kapin would be expected to induce lowering of intraocular pressure is associated with their vasodilatory properties. For example, the principal and primary antiglaucomatic therapy consists of topical application of beta-blockers, well-known vasodilators. Wallace Alward, Medical Management of Glaucoma, 339 NEJM 1298, 1301 (1998). Far from adversely contrasting the IOP lowering effects of fasudil, the addition of a rho kinase inhibitor could reasonably be expected to either improve the IOP lowering capacity of a prostaglandin derivative, or at the very least act to lessen potential IOP raising side effects associated with $PGF_{2\alpha}$ anti-glaucomatics such as those taught by Bito.

Applicant arguments concerning difficulties associated with drug combinations for the treatment of diseases such as glaucoma fail for at least two reasons: As a threshold matter, applicants have offered no objective evidence establishing this premise, a result of which is that the entirety of the argument is attorney opinion, entitled to no evidentiary weight. MPEP 2145(I). Secondly, combination therapeutics for the treatment of glaucoma are well known, and any difficulties associated with combination treatments are well within the ability of a skilled artisan to handle. See P.F. Hoyng & L.M. van Beek, Pharmacological Therapy for Glaucoma: A Review, 59 DRUGS 411 (March 2000) (indicating combination therapy is commonly employed when monotherapy has failed to provide a desired therapeutic outcome)

Applicants are reminded that obviousness necessarily take into consideration the total knowledge possessed by the skilled artisan, not merely the information conveyed by an individual reference. As such, in the context of an obviousness rejection, arguments directed to the disclosure of references individually cannot serve to overcome an obviousness rejection. MPEP § 2145(IV). Where multiple references from analogous art each teach individual elements of a claimed invention, and the examiner provides a rationale which the skilled artisan at the time of the invention claimed could have employed to unite the individual teachings of the relied upon references, a prima facie case of obviousness is established. KSR International Co. v. Teleflex, Inc., 127 S.Ct. 1727, 1740 (2007) Such a prima facie case can only be overcome by amending the claims to exclude the relied upon art, or, by proper submission of objective indicia of nonobviousness commensurate in scope with the invention claimed, demonstrate some degree of unexpected results were obtained by the combination claimed. MPEP § 716, et seq. Such unexpected results must indeed be unexpected by the skilled artisan, and must be determined in

comparison to the closest art which actually exists. Id. Here, the only objective data applicants have repeatedly provided relies on comparisons to the individual components of the combination composition in relation to a placebo control and to the individual elements of the combination composition, using only two of the four claimed prostaglandins. This evidence cannot form the basis of a determination that the claimed combination presents unexpected results, as not only have applicants failed to compare the claimed invention to the closest prior art, they have also failed to demonstrate the improvement in the IOP lowering result of the combination is in fact unexpected. As discussed in both the Alward and Hoyng references disclosed above, in the treatment of glaucoma combination therapy is commonly employed in situations where monotherapy has been proven to be insufficient in providing the desired therapeutic result. The skilled artisan would therefore expect improved IOP lowering results when combining IOP lowering agents. Even given these expectations, from the data presented it appears that the applicants claimed combination of a prostaglandin and rho kinase inhibitor provides less than additive reduction of intraocular pressure when compared to either component given alone. As such, no objective evidence in support of nonobviousness has been made of record, and the examiner's rejection shall stand.

Conclusion

No Claims stand allowable.

This is an RCE of applicant's earlier Application No. 10/525,986. All claims are drawn to the same invention claimed in the earlier application and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the earlier

application. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action in this case. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no, however, event will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SEAN BASQUILL whose telephone number is (571)270-5862. The examiner can normally be reached on Monday through Thursday, between 8AM and 6PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brian Kwon can be reached on (571) 272-0581. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/KARLHEINZ R SKOWRONEK/
Primary Examiner, Art Unit 1631

/Sean Basquill/
Examiner, Art Unit 1613